

09/16/2004
part of Dialog search

Set	Items	Description
S1	125	THYMIDYLATE (20N) (POLYMORPH? OR REPEAT)
S2	46	RD (unique items)
S3	28	S2 NOT PY>=1999
S4	2	S2 (20N) (DRUG OR THERAP?)
S5	1959	THYMIDYLATE (20N) EXPRESSION
S6	2176	THYMIDYLATE (20N) EXPRESS?
S7	528	S6 (20N) (CANCER OR TUMOR)
S8	68	S7 (20N) (DRUG OR THERAP?)
S9	44	RD (unique items)
S10	28	S9 NOT PY>=1999

? s s10 not s3

28 S10

28 S3

S11 27 S10 NOT S3

? t 11/5/all

11/5/1 (Item 1 from file: 34)
DIALOG(R) File 34:SciSearch(R) Cited Ref Sci
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07002680 Genuine Article#: 113TM Number of References: 15
Title: Thymidylate synthase as a predictor of response
Author(s): Leichman CG (REPRINT)
Corporate Source: ROSWELL PK CANC INST, DIV MED, ELM & CARLTON
ST/BUFFALO//NY/14263 (REPRINT)
Journal: ONCOLOGY-NEW YORK, 1998, V12, N8, 6 (AUG), P43-47
ISSN: 0890-9091 Publication date: 19980800
Publisher: P R R INC, 17 PROSPECT ST, HUNTINGTON, NY 11743
Language: English Document Type: ARTICLE
Geographic Location: USA
Subfile: CC CLIN--Current Contents, Clinical Medicine
Journal Subject Category: ONCOLOGY
Abstract: It has been hypothesized that intratumoral %thymidylate% synthase (TS) gene %expression% might be used to select %therapy% for patients with disseminated colorectal %cancer%. We recently reported the results of a clinical trial in 46 patients with disseminated or recurrent colorectal cancer testing whether expression of TS within the primary tumor, as assessed by quantitative polymerase chain reaction (PCR) methodology, would predict the responsiveness of that cancer to fluoropyrimidine-based therapy. This trial demonstrated that intratumoral TS/beta-actin messenger RNA (mRNA) ratio can accurately predict which metastatic colorectal tumors will be resistant to a leucovorin-modulated 5-FU infusion and which have a high likelihood of responding to such a regimen. Results of other studies of adjuvant therapy in gastric cancer and colorectal cancer also indicated that TS expression within the tumor is predictive of response to 5-FU-based therapy. It may be possible to use this parameter prospectively to decide which patients should receive fluorinated pyrimidine therapy: Patients whose tumors express low TS levels would be likely to benefit from such therapy, whereas limited preliminary data suggest that patients whose tumors express high TS levels may benefit from irinotecan (CPT-11 [Camptosar]).

Identifiers--KeyWord Plus(R): DISSEMINATED COLORECTAL-CANCER;
PROTRACTED-INFUSION; WEEKLY LEUCOVORIN; EXPRESSION; QUANTITATION;
FLUOROURACIL

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11/5/2 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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06705273 Genuine Article#: ZL982 Number of References: 49
Title: Restoration of wild-type p53 activity in p53-null HL-60 cells
confers multidrug sensitivity
Author(s): Ju JF; Banerjee D; Lenz HJ; Danenberg KD; Schmittgen TC; Spears
CP; Schonthal AH; Manno DJ; Hochhauser D; Bertino JR; Danenberg PV
(REPRINT)
Corporate Source: UNIV SO CALIF, SCH MED, NORRIS COMPREHENS CANC CTR, 1303 N
MISSION RD/LOS ANGELES//CA/90033 (REPRINT); UNIV SO CALIF, SCH MED,
NORRIS COMPREHENS CANC CTR/LOS ANGELES//CA/90033; MEM SLOAN KETTERING
CANC CTR,/NEW YORK//NY/10021
Journal: CLINICAL CANCER RESEARCH, 1998, V4, N5 (MAY), P1315-1322
ISSN: 1078-0432 Publication date: 19980500
Publisher: AMER ASSOC CANCER RESEARCH, PO BOX 11806, BIRMINGHAM, AL 35202
Language: English Document Type: ARTICLE
Geographic Location: USA
Subfile: CC CLIN--Current Contents, Clinical Medicine
Journal Subject Category: ONCOLOGY
Abstract: HL-60 cells that stably express transfected wild-type (wt) p53
were used to determine whether restoration of wt p53 increased the
chemosensitivity of cells that normally lack p53 activity. The wt p53
HL-60 transfectants (SN3 cells) were more sensitive than the parental
(S) cells to a number of common anticancer drugs representing various
mechanisms of action, whereas HL-60 cells transfected with p53 genes
mutated at codons 248 and 143 were not sensitized. The sensitization
ratio due to the transfected wt p53 varied from about 2-fold for
cisplatin to over 50-fold for thymidine. Cells treated with the
thymidylate synthase inhibitor 5-fluoro-2'-deoxyuridine (FdUrd) were
used to study changes in various p53-associated gene expressions. A
higher percentage of apoptotic cells among the SN3 cells was observed
than among the S cells at each concentration of FdUrd. The S cells had
undetectable levels of bar and high levels of bcl-2, whereas the SN3
cells had undetectable levels of bcl-2 levels and appreciable basal
levels of bar. After FdUrd treatment of SN3 cells, both p53 and bar
levels increased, but the induction of bar was faster than that of p53
and paralleled the appearance of apoptotic DNA laddering. FdUrd
treatment induced p21 expression and increased the G(1) fraction of the
SN3 cells but did not induce p21 or change the phase distribution in
the S cells. FdUrd treatment also induced the expression and
phosphorylation of cyclin D1 in the SN3 cells but not in the S cells.
These results show that transfected wt p53 confers multidrug
sensitivity to HL-60 cells by re-adjustment of the expressions of
apoptosis genes and displays other properties characteristic of
endogenously originated wt p53.

Identifiers--KeyWord Plus(R): %TUMOR%-SUPPRESSOR GENE; ADENOVIRUS-MEDIATED

TRANSFER; %THERAPY% IN-VIVO; %CANCER% CELLS; CYCLE CONTROL;
%THYMIDYLATE% SYNTHASE; NECK-%CANCER%; DNA-DAMAGE; BAX GENE;
%EXPRESSION%

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11/5/3 (Item 3 from file: 34)

DIALOG(R) File 34:SciSearch(R) Cited Ref Sci
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06619996 Genuine Article#: ZF220 Number of References: 24
Title: Higher levels of thymidylate synthase gene expression are observed
in pulmonary as compared with hepatic metastases of colorectal
adenocarcinoma
Author(s): Gorlick R; Metzger R; Danenberg KD; Salonga D; Miles JS; Longo
GSA; Fu J; Banerjee D; Klimstra D; Jhanwar S; Danenberg PV; Kemeny N;

Bertino JR (REPRINT)
Corporate Source: MEM SLOAN KETTERING CANC CTR, DEPT PEDIAT, PROGRAM MOL PHARMACOL & THERAPEUT, 1275 YORK AVE, BOX 78/NEW YORK//NY/10021 (REPRINT); MEM SLOAN KETTERING CANC CTR, DEPT PEDIAT, PROGRAM MOL PHARMACOL & THERAPEUT/NEW YORK//NY/10021; MEM SLOAN KETTERING CANC CTR, DEPT PATHOL/NEW YORK//NY/10021; MEM SLOAN KETTERING CANC CTR, DEPT HUMAN GENET/NEW YORK//NY/10021; MEM SLOAN KETTERING CANC CTR, DEPT MED/NEW YORK//NY/10021; MEM SLOAN KETTERING CANC CTR, DEPT MOL PHARMACOL/NEW YORK//NY/10021; MEM SLOAN KETTERING CANC CTR, DEPT EXPT THERAPEUT/NEW YORK//NY/10021; UNIV SO CALIF, KENNETH NORRIS JR COMPREHENS CANC CTR/LOS ANGELES//CA/90033

Journal: JOURNAL OF CLINICAL ONCOLOGY, 1998, V16, N4 (APR), P1465-1469

ISSN: 0732-183X Publication date: 19980400

Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399

Language: English Document Type: ARTICLE

Geographic Location: USA

Subfile: CC LIFE--Current Contents, Life Sciences; CC CLIN--Current Contents, Clinical Medicine;

Journal Subject Category: ONCOLOGY

Abstract: Purpose: It has been observed previously that the pulmonary metastases of colorectal adenocarcinoma are less responsive to therapy with fluorouracil (FUra) as compared with other sites of metastasis (liver, local). To investigate the basis of this chemoresistance, the levels of %thymidylate% synthase (TS) mRNA and protein were measured, as TS %expression% has been shown to be predictive of response to %therapy% in colorectal %cancer%.

Materials and Methods: Tumors were obtained from 19 patients with metastatic colorectal cancer(12 hepatic and seven pulmonary). TS expression was measured by quantitative reverse-transcriptase polymerase chain reaction (RT-PCR) and TS protein levels were measured by Western blotting. The presence of TS amplification was assessed by Southern blotting. Levels of p53 protein were determined using immunohistochemistry.

Results: TS mRNA expression was shown to be significantly higher in the pulmonary metastases (mean TS/beta-actin ratio, 19.7; n = 7) as compared with the hepatic metastases (mean TS/beta-actin ratio, 4.7; n = 11) of colorectal cancer. Lower TS expression was observed in patients with hepatic metastases who had received prior FUra versus patients who had not been treated. High levels of TS expression in some samples was associated with low-level (two to three gene copies) increases in TS gene copy numbers and this was observed more frequently in the pulmonary metastatic samples. The increased gene copy numbers occurred both in samples with wild-type p53 and those with mutant p53 tumor-suppressor gene as determined by immunohistochemistry.

Conclusion: High levels of TS enzyme may be the basis of the lack of response of pulmonary metastases to FUra treatment. (C) 1998 by American Society of Clinical Oncology.

Identifiers--KeyWord Plus(R): WILD-TYPE P53; DIHYDROFOLATE-REDUCTASE; CANCER; AMPLIFICATION; RESISTANCE; SURVIVAL; QUANTITATION; PREDICTOR; CARCINOMA; TUMORS

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11/5/4 (Item 4 from file: 34)
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05121552 Genuine Article#: BG03K Number of References: 69
Title: THE ROLE OF THYMIDYLATE SYNTHASE IN CELLULAR-REGULATION
Author(s): CHU E; ALLEGRA CJ
Corporate Source: NCI,USN,MED ONCOL BRANCH/BETHESDA//MD/20889
Journal: ADVANCES IN ENZYME REGULATION, 1996, V36, P143-163
ISSN: 0065-2571
Language: ENGLISH Document Type: REVIEW
Geographic Location: USA
Subfile: ISTP; SciSearch
Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY
Identifiers--KeyWords Plus: COLON-CANCER-CELLS; TRANSFER-RNA SYNTHETASE;
TUMOR-SUPPRESSOR GENE; KINASE MESSENGER-RNA; DIHYDROFOLATE-REDUCTASE;
ESCHERICHIA-COLI; THYMIDINE KINASE; BINDING-SITE; MOUSE FIBROBLASTS;
BREAST-CANCER
Research Fronts: 94-1131 004 (HIGH-DOSE 5-FLUOROURACIL 24-HOUR INFUSION;
FOLINIC ACID; METASTATIC COLORECTAL-CARCINOMA; PHASE-II TRIAL;
LEUCOVORIN %THERAPY%; HEPATIC ARTERIAL CHEMOTHERAPY)
94-6279 002 (P53 %TUMOR%-SUPPRESSOR GENE; EXHIBIT NORMAL G1 CELL-CYCLE
ARREST; POSTTRANSLATIONAL REGULATION)
94-1893 001 (P53 PROTEIN; %EXPRESSION% IN MALIGNANT-MELANOMA;
CARCINOGENESIS OF ESOPHAGEAL SQUAMOUS-CELL CARCINOMA)
94-5042 001 (%THYMIDYLATE% SYNTHASE; MOUSE WHEY ACIDIC PROTEIN PROMOTER
HUMAN GROWTH-HORMONE (MWAP/HGH) TRANSGENIC MICE; HHAL METHYLTRANSFERASE
FLIPS)
94-6508 001 (TRANSLATION INITIATION; REGULATION OF EIF-2 ALPHA-SUBUNIT
PHOSPHORYLATION; S-ADENOSYLMETHIONINE DECARBOXYLASE MESSENGER-RNA;
5'-UNTRANSLATED REGION)
94-7136 001 (IRON-RESPONSIVE ELEMENT-BINDING PROTEIN;
POSTTRANSCRIPTIONAL REGULATION; 3' UNTRANSLATED REGION; TRANSFERRIN
RECEPTOR GENE-EXPRESSION)

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11/5/5 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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04685417 Genuine Article#: UA994 Number of References: 66
Title: THE VOLE OF THYMIDYLATE SYNTHASE AS AN RNA-BINDING PROTEIN
Author(s): CHU E; ALLEGRA CJ
Corporate Source: USN, NCI, MED ONCOL BRANCH/BETHESDA//MD/20889

Journal: BIOESSAYS, 1996, V18, N3 (MAR), P191-198

ISSN: 0265-9247

Language: ENGLISH Document Type: REVIEW

Geographic Location: USA

Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences

Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY

Abstract: Thymidylate synthase plays a central role in the biosynthesis of thymidylate, an essential precursor for DNA biosynthesis. In addition to its role in catalysis and cellular metabolism, it is now appreciated that thymidylate synthase functions as an RNA binding protein. Specifically, thymidylate synthase binds with high affinity to its own mRNA, resulting in translational repression. An extensive series of experiments has been performed to elucidate the molecular elements underlying the interaction between thymidylate synthase and its own mRNA. In addition to characterization of the underlying cis- and trans-acting elements, recent studies have shown that thymidylate synthase has the capacity to bind specifically to other cellular RNA species. While the biological significance of these other RNA/thymidylate synthase interactions remains to be defined, this work suggests a potential role for TS in coordinately regulating several critical aspects of cellular metabolism.

Identifiers--KeyWords Plus: 3' UNTRANSLATED REGION; MESSENGER-RNA; ESCHERICHIA-COLI; NUCLEOTIDE-SEQUENCE; MOUSE FIBROBLASTS; R17-COAT PROTEIN; COAT PROTEIN; POLY(A) TAIL; CELL-LINE; TRANSLATION

Research Fronts: 94-1131 002 (HIGH-DOSE 5-FLUOROURACIL 24-HOUR INFUSION; FOLINIC ACID; METASTATIC COLORECTAL-CARCINOMA; PHASE-II TRIAL; LEUCOVORIN %THERAPY%; HEPATIC ARTERIAL CHEMOTHERAPY)

94-3689 002 (AU-RICH 3' UNTRANSLATED REGION OF MESSENGER-RNA; GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR %EXPRESSION%; RAT LIPOPOLYSACCHARIDE-BINDING PROTEIN)

94-5042 001 (%THYMIDYLATE% SYNTHASE; MOUSE WHEY ACIDIC PROTEIN PROMOTER HUMAN GROWTH-HORMONE (MWAP/HGH) TRANSGENIC MICE; HHAL METHYLTRANSFERASE FLIPS)

94-6279 001 (P53 %TUMOR%-SUPPRESSOR GENE; EXHIBIT NORMAL G1 CELL-CYCLE ARREST; POSTTRANSLATIONAL REGULATION)

94-7136 001 (IRON-RESPONSIVE ELEMENT-BINDING PROTEIN; POSTTRANSCRIPTIONAL REGULATION; 3' UNTRANSLATED REGION; TRANSFERRIN RECEPTOR GENE-EXPRESSION)

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11/5/6 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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03887805 Genuine Article#: QP339 Number of References: 42
Title: MESSENGER-RNA EXPRESSION OF RESISTANCE FACTORS AND THEIR CORRELATION
TO THE PROLIFERATIVE ACTIVITY IN CHILDHOOD ACUTE LYMPHOBLASTIC-LEUKEMIA
Author(s): STAMMLER G; SAUERBREY A; VOLM M
Corporate Source: GERMAN CANC RES CTR,DEPT 0511,NEUENHEIMER FELD 280,POB
101949/D-69009 HEIDELBERG//GERMANY//; GERMAN CANC RES CTR,DEPT
0511/D-69009 HEIDELBERG//GERMANY//; UNIV JENA,CHILDRENS HOSP/O-6900
JENA//GERMANY//
Journal: CANCER LETTERS, 1995, V89, N1 (FEB 10), P129-135
ISSN: 0304-3835
Language: ENGLISH Document Type: ARTICLE
Geographic Location: GERMANY
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: ONCOLOGY
Abstract: In this report we analyzed the mRNA expression of the
resistance-related enzymes DNA topoisomerase II (Topo II), thymidylate
synthase (TS), glutathione S-transferase-pi (GST-pi) and glutathione
peroxidase (GP) in childhood acute lymphoblastic leukemia (ALL) and
their correlation to the proliferative activity, determined by Ki-67.

RNA of blast cells from 54 children with untreated ALL were examined by dot blot hybridization. We found a significant positive correlation between Topo II and TS and cell proliferation. No significant correlation was detected between the mRNA expression of the glutathione-dependent enzymes GST-pi or GP and Ki-67. The results were substantiated by a semiquantitative RT-PCR-assay and by immunocytochemistry.

Descriptors--Author Keywords: DNA TOPOISOMERASE II ; THYMIDYLATE SYNTHASE ; GLUTATHIONE S-TRANSFERASE-PI ; GLUTATHIONE PEROXIDASE ; KI-67 ; PROLIFERATION ; ACUTE LYMPHOBLASTIC LEUKEMIA

Identifiers--KeyWords Plus: DNA TOPOISOMERASE-II; BREAST %CANCER%-CELLS; %THYMIDYLATE% SYNTHASE; %TUMOR%-CELLS; ELEVATED %EXPRESSION%; %DRUG%-RESISTANCE; ANTITUMOR DRUGS; PROGNOSIS; GENE; METHOTREXATE

Research Fronts: 93-3952 002 (MAMMALIAN DNA TOPOISOMERASE-II; ANTITUMOR AGENTS; POTENT INHIBITORS)

93-1657 001 (THYMIDYLATE SYNTHASE; PRENEOPLASTIC MAMMARY HYPERPLASTIC ALVEOLAR NODULES OF SHN VIRGIN MICE; 5-FLUOROURACIL GASTROINTESTINAL TOXICITY IN RATS)

93-1977 001 (GLUTATHIONE S-TRANSFERASES; ADULT TOAD (BUFO-BUFO) LIVER; MAMMALIAN THETA-CLASS ISOENZYMES)

93-3155 001 (PROLIFERATING CELL NUCLEAR ANTIGEN; PROGNOSTIC IMPACT IN ARCHIVAL PARAFFIN-EMBEDDED NODE-NEGATIVE BREAST-CANCER; IMMUNOHISTOCHEMICAL EVIDENCE)

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11/5/7 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02050030 Genuine Article#: JW768 Number of References: 106
Title: DRUG-RESISTANCE IN ONCOLOGY - FROM CONCEPTS TO APPLICATIONS
Author(s): CAZIN JL; GOSSELIN P; CAPPELAERE P; ROBERT J; DEMAILLE A
Corporate Source: CTR OSCAR LAMBRET, RADIOPHARM & ONCOPHARMACOL LAB, 1 RUE F
COMBEMALE, BP 307/F-59020 LILLE//FRANCE//; FDN BERGONIE, BIOCHIM
LAB/F-33076 BORDEAUX//FRANCE//
Journal: JOURNAL OF CANCER RESEARCH AND CLINICAL ONCOLOGY, 1992, V119, N2 (NOV), P76-86

ISSN: 0171-5216

Language: ENGLISH Document Type: EDITORIAL

Geographic Location: FRANCE

Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences

Journal Subject Category: ONCOLOGY

Abstract: The complex problem of drug resistance is discussed with respect to host toxicity, to tumor characteristics (kinetic resistance, heterogeneity of cell subpopulations, hypoxia, mutation and gene amplification), and to the medication itself (pharmacokinetic and pharmacodynamic resistance: cell membrane, intracellular metabolism, intracellular target). After detailing each type of resistance, the possibilities of fighting against drug resistance are explored (dealing with host toxicity, tumor characteristics and drugs - intensifying therapy, multiple drug therapy, biochemical modulation, particular modalities of drug administration). Finally, perspectives of research and development of new drugs are summarized.

Descriptors--Author Keywords: ONCOPHARMACOLOGY ; RESISTANCE TO CHEMOTHERAPY ; PGP ; GST ; TOPOISOMERASES

Identifiers--KeyWords Plus: BACTERIAL TRANSPORT PROTEINS; P-GLYCOPROTEIN EXPRESSION; DOUBLE MINUTE CHROMOSOMES; CANCER CELL-LINES; MULTIDRUG-RESISTANCE; MONOCLONAL-ANTIBODIES; ANTICANCER DRUGS; LEUKEMIA-CELLS; CYTO-TOXICITY; CONFERS RESISTANCE

Research Fronts: 90-0790 012 (MULTIDRUG RESISTANCE; P-GLYCOPROTEIN %EXPRESSION%; ACTIVITY OF VERAPAMIL)
90-2128 001 (%THYMIDYLATE% SYNTHASE; CONTINUOUS INFUSION HIGH-DOSE LEUCOVORIN; 5-FLUOROURACIL ACTIVITY; FOLINIC ACID; COLON %CANCER%)
90-2380 001 (PHOTODYNAMIC %THERAPY%; %TUMOR% FACTORS IN CANCER METASTASIS; HEMATOPORPHYRIN DERIVATIVE; INVIVO GROWTH)
90-3635 001 (MOLECULAR EVOLUTION OF THE ESCHERICHIA-COLI CHROMOSOME; HOMOLOGOUS RECOMBINATION; ADAPTIVE MUTATIONS; BACTERIAL OPERON; RIF-1 TUMORS; CANCER METASTASIS)
90-6024 001 (CHEMOTHERAPY OF HODGKINS-DISEASE; LIMITED STAGE SMALL-CELL LUNG-CANCER; NO MAINTENANCE THERAPY)
90-6295 001 (CISPLATIN RESISTANCE; DNA INTERACTIVE ANTICANCER DRUGS; REDUCED GLUTATHIONE; HUMAN OVARIAN-CARCINOMA CELLS; N-15-[H-1] DEPT NMR)

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11/5/8 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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09745479 BIOSIS NO.: 199598200397
Alteration of metallothionein or %thymidylate% synthase %expression% in
human %tumor% cells: Effects on %drug% resistance.
AUTHOR: Demoor J; Koropatnick J; Vincent M; Sharpe J; Vertesi V; Collins O;
Leibbrandt M; Fraser J
AUTHOR ADDRESS: London Regional Cancer Centre, London N6A 4L6**Canada
JOURNAL: Proceedings of the American Association for Cancer Research Annual
Meeting 36 (0):p321 1995
CONFERENCE/MEETING: Eighty-sixth Annual Meeting of the American Association
for Cancer Research Toronto, Ontario, Canada March 18-22, 1995
ISSN: 0197-016X
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 9031-61-2: THYMIDYLATE SYNTHASE; 15663-27-1: CISPLATIN;
305-03-3: CHLORAMBUCIL; 7440-43-9: CADMIUM

DESCRIPTORS:
MAJOR CONCEPTS: Enzymology (Biochemistry and Molecular Biophysics);
Metabolism; Oncology (Human Medicine, Medical Sciences); Pharmacology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata,
Animalia
ORGANISMS: Hominidae (Hominidae)
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): animals; chordates; humans;
mammals; primates; vertebrates
CHEMICALS & BIOCHEMICALS: THYMIDYLATE SYNTHASE; CISPLATIN; CHLORAMBUCIL
; CADMIUM
MISCELLANEOUS TERMS: ANTINEOPLASTIC-DRUG; CADMIUM; CHLORAMBUCIL;
CISPLATIN; DRUG RESISTANCE MECHANISMS; IONIZING RADIATION; MEETING
ABSTRACT; METAL HOMEOSTASIS

CONCEPT CODES:
10808 Enzymes-Physiological Studies
13010 Metabolism-Minerals

22002 Pharmacology-General
24006 Neoplasms and Neoplastic Agents-Biochemistry
24008 Neoplasms and Neoplastic Agents-Therapeutic Agents; Therapy
00520 General Biology-Symposia, Transactions and Proceedings of
Conferences, Congresses, Review Annuals
02506 Cytology and Cytochemistry-Animal
06504 Radiation-Radiation and Isotope Techniques
06506 Radiation-Radiation Effects and Protective Measures
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
10069 Biochemical Studies-Minerals

BIOSYSTEMATIC CODES:

86215 Hominidae

11/5/9 (Item 1 from file: 155)
DIALOG(R) File 155: MEDLINE(R)
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09856197 98384332 PMID: 9716444
Antisense nucleic acids targeted to the thymidylate synthase (TS) mRNA
translation start site stimulate TS gene transcription.
DeMoor JM; Vincent MD; Collins OM; Koropatnick J
The London Regional Cancer Centre, 790 Commissioners Road East, London,
Ontario, N6A 4L6, Canada.

Experimental cell research (UNITED STATES) Aug 25 1998, 243 (1)
p11-21, ISSN 0014-4827 Journal Code: EPB

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Subfile: INDEX MEDICUS

Thymidylate synthase (TS) is a key enzyme in the synthesis of DNA and a target for cancer chemotherapeutic agents. Antisense TS nucleic acids may be useful in enhancing anticancer drug effectiveness. MCF-7 and HeLa cells were transfected with vectors expressing antisense TS RNA or with antisense oligodeoxynucleotides (AS-ODNs) to different TS mRNA regions. Antisense RNAs were targeted to 30 bases of the TS mRNA including part of the stem loop at the translation start site and to 30 bases spanning the exon1/exon2 boundary. AS-ODNs were targeted to the translation start site and the translation stop site. Antisense nucleic acids complementary to the translation start site (and not the exon1/exon2 boundary or translation stop site) significantly enhanced constitutive TS gene transcription. Therefore, TS mRNA sequences appear to be involved in a novel pathway controlling TS gene transcription. Induced transcription could hinder antisense-based attempts to inhibit TS and must be considered when designing such strategies. Copyright 1998 Academic Press.

Tags: Human; Support, Non-U.S. Gov't

Descriptors: *RNA, Antisense--pharmacology--PD; *Thymidylate Synthase--genetics--GE; Blotting, Northern; Blotting, Southern; Breast Neoplasms--genetics--GE; Breast Neoplasms--metabolism--ME; Down-Regulation (Physiology); Gene %Expression%--%drug% effects--DE; Hela Cells--metabolism--ME; Oligonucleotides, Antisense--pharmacology--PD; RNA, Messenger--analysis--AN; %Thymidylate% Synthase--%drug% effects--DE; Transcription, Genetic--%drug% effects--DE; Transfection; %Tumor% Cells, Cultured

CAS Registry No.: 0 (Oligonucleotides, Antisense); 0 (RNA, Antisense); 0 (RNA, Messenger)

Enzyme No.: EC 2.1.1.45 (Thymidylate Synthase)

Record Date Created: 19980924

11/5/10 (Item 2 from file: 155)
DIALOG(R) File 155: MEDLINE(R)
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09792875 98324629 PMID: 9662252
Thymidylate synthase expression and activity: relation to S-phase

parameters and 5-fluorouracil sensitivity.

Mirjolet JF; Barberi-Heyob M; Merlin JL; Marchal S; Etienne MC; Milano G; Bey P

Centre Alexis Vautrin, Laboratoire de Recherche en Oncologie, Vandoeuvre-les-Nancy, France.

British journal of cancer (SCOTLAND) Jul 1998, 78 (1) p62-8, ISSN 0007-0920 Journal Code: AV4

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Subfile: INDEX MEDICUS

Six human cancer cell lines exhibiting a large range of sensitivity to 5-fluorouracil (5-FU) were evaluated for thymidylate synthase (TS) and p53 gene expression, TS and dihydropyrimidine dehydrogenase (DPD) activity, as well as cell cycle parameters, S-phase fraction (SPF), bromodeoxyuridine labelling index (LI) and S-phase duration (SPD). All these parameters were investigated for 7 days in asynchronously growing cell populations and compared with the cell sensitivity to 5-FU. No significant correlation was found between S-phase parameters and TS gene expression and/or activity. TS activity was higher in proliferating cells; however, it was not significantly higher in rapidly growing cell lines with short SPD. Neither TS gene expression nor activity was found to correlate with 5-FU sensitivity. On the other hand, a statistically significant correlation ($P < 0.0001$) was observed between LI and SPD and 5-FU sensitivity. The present results suggest that cell cycle parameters such as SPD and/or LI could be better parameters for 5-FU sensitivity prediction than TS gene expression and/or activity. This could be especially informative in cases of concomitant radio-chemotherapy as S-phase parameters are already proposed for hyperfractionated radiotherapy planning.

Tags: Human; Support, Non-U.S. Gov't

Descriptors: *Antimetabolites, Antineoplastic--pharmacology--PD; *Fluorouracil--pharmacology--PD; *Neoplasm Proteins--metabolism--ME; *S Phase--physiology--PH; *Thymidylate Synthase--metabolism--ME; Cell Division --%drug% effects--DE; Gene %Expression% Regulation, Enzymologic; Neoplasm Proteins--genetics--GE; Oxidoreductases--metabolism--ME; %Thymidylate% Synthase--genetics--GE; %Tumor% Cells, Cultured--%drug% effects--DE

CAS Registry No.: 0 (Antimetabolites, Antineoplastic); 0 (Neoplasm Proteins); 51-21-8 (Fluorouracil)

Enzyme No.: EC 1. (Oxidoreductases); EC 1.3.1.2 (dihydrouracil dehydrogenase(NADP)); EC 2.1.1.45 (Thymidylate Synthase)

Record Date Created: 19980720

11/5/11 (Item 3 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

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09401651 97309778 PMID: 9167189

Determinants of cytotoxicity with prolonged exposure to fluorouracil in human colon cancer cells.

Ren Q; Van Groeningen CJ; Hardcastle A; Aherne GW; Geoffroy F; Allegra CJ; Johnston PG; Grem JL

Developmental Therapeutics Department, National Cancer Institute, National Naval Medical Center, Bethesda, MD 20889-5105, USA.

Oncology research (UNITED STATES) 1997, 9 (2) p77-88, ISSN 0965-0407 Journal Code: BBN

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Subfile: INDEX MEDICUS

To explore the determinants of cytotoxicity during prolonged exposure to pharmacologically relevant concentrations of 5-fluorouracil (FUra), we studied the effects of FUra at concentrations ranging from 0.1 to 1 microM in HCT 116 and HT 29 colon cancer cells grown in the presence of physiologic levels of leucovorin. A 5- and 7-day exposure to 1 microM FUra

reduced cell growth to 46% and 20% of control in HT 29 cells and to 74% and 38% of control in HCT 116 cells. Concurrent exposure to thymidine (10 or 20 microM) or uridine (1 mM) provided partial protection against FUra toxicity in HT 29 cells, but did not protect HCT 116 cells. After a 24-h exposure to 1 microM [³H]FUra, free 5-fluoro-2'-deoxyuridine-5'-monophosphate (FdUMP) and FUDP + FUTP levels were 0.7 and 144 pmol/10(6) cells in HT 29 cells, respectively, and 3.9 and 178 pmol/10(6) cells in HCT 116 cells. FdUMP and FUDP + FUTP pools increased by 5.7- and 2.0-fold in HT 29 cells and by 1.7- and 3.3-fold in HCT 116 cells over the next 48 h, but did not accumulate thereafter. After a 24-h exposure to 1 microM [³H]FUra, FUra-RNA levels were 158 and 280 fmol/microgram in HT 29 and HCT 116 cells, respectively; FUra-RNA levels increased over time, and reached 700 and 1156 fmol/microgram at day 5. Concurrent exposure to 1 mM uridine for 72 h did not diminish [³H]FUra-RNA incorporation. Upon removal of [³H]FUra following a 24-h exposure, FUra-RNA levels remained relatively stable with 57-78% retained at 120 h. A low level of [³H]FUra-DNA incorporation was detected in HT 29 cells. Thymidylate synthase (TS) catalytic activity in control cells was 2-fold higher in HCT 116 cells compared to HT 29 cells (47 vs. 23 pmol/min/mg). Total TS content increased 1.5- to 3-fold over control in both cell lines during FUra exposure, and ternary complex formation was evident for up to 96 h-dTTP pools were not depleted in FUra-treated cells, suggesting that residual TS catalytic activity was sufficient to maintain dTTP pools relative to demand. Surprisingly, the partial inhibition of TS was accompanied by a striking accumulation of immunoreactive "dUMP" pools in both lines; dUTP pools also increased 2-to 3-fold. In summary, the gradual and stable accumulation of FUra in RNA noted in both lines may account for the thymidine-insensitive component of FUra toxicity. Because dTTP pools were not appreciably diminished, the interference with nascent DNA chain elongation and induction of single-strand breaks in newly synthesized DNA in both cell lines may be due to misincorporation of deoxyuridine nucleotides.

Tags: Human

Descriptors: *Cell Survival--drug effects--DE; *DNA Damage; *Fluorouracil --toxicity--TO; *Leucovorin--pharmacology--PD; Cell Division--drug effects --DE; Colonic Neoplasms; DNA, Neoplasm--%drug% effects--DE; Deoxyribonucleotides--metabolism--ME; Deoxyuracil Nucleotides--metabolism --ME; Dose-Response Relationship, %Drug%; Fluorodeoxyuridylate--metabolism --ME; Fluorouracil--metabolism--ME; Gene %Expression% Regulation, Enzymologic--%drug% effects--DE; %Thymidylate% Synthase--antagonists and inhibitors--AI; %Thymidylate% Synthase--biosynthesis--BI; %Tumor% Cells, Cultured; Uridine Triphosphate--analogs and derivatives--AA; Uridine Triphosphate--metabolism--ME

CAS Registry No.: 0 (5-fluoro-2'-deoxyuridine-5'-diphosphate); 0 (DNA, Neoplasm); 0 (Deoxyribonucleotides); 0 (Deoxyuracil Nucleotides); 134-46-3 (Fluorodeoxyuridylate); 3828-96-4 (5-fluorouridine 5'-triphosphate); 51-21-8 (Fluorouracil); 58-05-9 (Leucovorin); 63-39-8 (Uridine Triphosphate)

Enzyme No.: EC 2.1.1.45 (Thymidylate Synthase)

Record Date Created: 19970710

11/5/12 (Item 4 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

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08766826 95226450 PMID: 7711067

Isolation and expression of rat thymidylate synthase cDNA: phylogenetic comparison with human and mouse thymidylate synthases.

Ciesla J; Weiner KX; Weiner RS; Reston JT; Maley GF; Maley F

Nencki Institute of Experimental Biology, Department of Cellular Biochemistry, Warsaw, Poland.

Biochimica et biophysica acta (NETHERLANDS) Apr 4 1995, 1261 (2)
p233-42, ISSN 0006-3002 Journal Code: A0W

Contract/Grant No.: CA44355, CA, NCI

Languages: ENGLISH

• Document type: Journal Article
Record type: Completed
Subfile: INDEX MEDICUS

Two cDNA clones representing rat hepatoma thymidylate synthase (rTS) were isolated from a lambda ZAP II cDNA library using as a probe a fragment of the human TS cDNA. The two were identical except that one was missing 50 bp and the other 23 bp corresponding to the 5' coding region of the protein. The missing region was obtained by screening a rat genomic library. The open reading frame of rTS cDNA encoded 921 bp encompassing a protein of 307 amino acids with a calculated molecular mass of 35,015 Da. Rat hepatoma TS appears identical to normal rat thymus TS and the two sequences differ from mouse TS in the same eight amino acid residues. Six of these differences are in the first 21 amino acids from the amino-end. The human enzyme differed from rat and mouse TS at 17 residues where the latter two were identical, with most changes being conservative in nature. The three species differed completely at only four sites. Because the mouse TS shares four amino acids with human TS at sites which differ from rTS and a comparable situation does not exist between rTS and human TS, it is suggested that mouse TS is closer to human TS phylogenetically than rTS. The polymerase chain reaction was used to subclone the protein coding region of rTS into a high expression vector, which expressed rTS in *Escherichia coli* to the extent of 10 to 20% of its cellular protein. Although the amino-end of the amplified TS was unblocked, that isolated from a FUDR-resistant rat hepatoma cell line contained mostly N-acetylmethionine on its N-terminal end, a finding that may have significant regulatory consequences, which are discussed. The TS level in the resistant cell line was 60 to 70-fold higher than normal which was found to be associated with both multiple gene copies and an expanded TS mRNA pool.

Tags: Animal; Comparative Study; Human; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Descriptors: *DNA, Complementary--isolation and purification--IP; *Thymidylate Synthase--genetics--GE; Amino Acid Sequence; Base Sequence; Carcinoma, Hepatocellular--genetics--GE; Cloning, Molecular; DNA, Complementary--metabolism--ME; %Drug% Resistance; *Escherichia coli* --metabolism--ME; Gene %Expression%; Mice; Molecular Sequence Data; Rats; Recombinant Proteins--genetics--GE; %Thymidylate% Synthase--metabolism--ME; %Tumor% Cells, Cultured

Molecular Sequence Databank No.: GENBANK/L12138

CAS Registry No.: 0 (DNA, Complementary); 0 (Recombinant Proteins)

Enzyme No.: EC 2.1.1.45 (Thymidylate Synthase)

Record Date Created: 19950515

11/5/13 (Item 5 from file: 155)
DIALOG(R) File 155: MEDLINE(R)
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08550725 95326357 PMID: 7602796

Rapid diagnosis of drug-resistant genes by PCR assay.

Funato T

Department of Clinical and Laboratory Medicine, Tohoku University School of Medicine, Sendai.

Rinsho byori (JAPAN) Jun 1995, 43 (6) p535-9, ISSN 0047-1860

Journal Code: KIV

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Subfile: INDEX MEDICUS

This report concerns the utility of the reverse transcription-polymerase chain reaction (RT-PCR) and quantitative PCR (QPCR) assay to detect the %drug%-resistance of related genes. The expression of some %drug%-resistance genes was compared with the sensitivity and resistance-acquired %cancer% cell lines to anti-%cancer% drugs by Northern blot analysis and PCR assay. The resistance cell lines exhibited an enhanced %expression% of

multi-%drug% resistance (MDR-1), %thymidylate% synthase (TS), c-fos and DNA polymerase beta genes. Then these genes that %expressed% mRNA were quantitated using RT-PCR. The expression of the genes was dependent on their sensitivity (IC50) to anti-%cancer% drugs. Additionally, the QPCR assay has been developed as a rapid method for the expression of %drug%-resistance genes and applied to the PCR products amplified by the RT-PCR. Thus the QPCR assay for the expression of genes will allow rapid detection of the drug-resistance to chemotherapy in human cancers.

Tags: Human

Descriptors: *Drug Resistance--genetics--GE; Blotting, Northern; Drug Resistance, Multiple--genetics--GE; Polymerase Chain Reaction--methods--MT
Record Date Created: 19950808

11/5/14 (Item 6 from file: 155)
DIALOG(R) File 155: MEDLINE(R)
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08033613 93233612 PMID: 8474431

Regulation of thymidylate synthase in human colon cancer cells treated with 5-fluorouracil and interferon-gamma.

Chu E; Koeller DM; Johnston PG; Zinn S; Allegra CJ

NCI-Navy Medical Oncology Branch, Bethesda, Maryland 20889.

Molecular pharmacology (UNITED STATES) Apr 1993, 43 (4) p527-33,

ISSN 0026-895X Journal Code: NGR

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Subfile: INDEX MEDICUS

The effects of fluorouracil (5-FU) and interferon-gamma (IFN-gamma) on the regulation of thymidylate synthase (TS) gene expression were investigated in the human colon cancer H630 cell line. By Western immunoblot analysis, TS protein levels in H630 cells were increased 3-, 5.5-, 5-, and 2.5-fold after 8-, 16-, 24-, and 36-hr exposure to 1 microM 5-FU, respectively. When H630 cells were exposed to varying concentrations of 5-FU (0.3-10 microM) for 24 hr, increases in TS protein up to 5.5-fold were observed. A 24-hr exposure to 1 microM 5-FU resulted in a 4.5-fold increase in the level of TS protein, whereas in 5-FU/IFN-gamma-treated cells TS protein was increased by only 1.8-fold, compared with control cells. IFN-gamma treatment alone did not affect TS protein levels, relative to control. Northern blot analysis revealed no changes in TS mRNA levels when H630 cells were exposed either to 1 microM 5-FU for 8-36 hr, to varying concentrations of 5-FU (0.3-10 microM) for 24 hr, or to the combination of 5-FU and IFN-gamma. Pulse-labeling studies with [³⁵S]methionine demonstrated a 3.5-fold increase in net synthesis of TS in cells treated with 1 microM 5-FU, whereas the level of newly synthesized TS increased only 1.5-fold in cells treated with 5-FU/IFN-gamma, compared with control cells. Pulse-chase studies revealed that the half-lives of TS protein in control and 5-FU-treated cells were equivalent. These findings demonstrate that the increase in TS protein after 5-FU exposure and the subsequent inhibitory effect of IFN-gamma on TS protein expression are both regulated at the post-transcriptional level.

Tags: Human

Descriptors: *Colonic Neoplasms--enzymology--EN; *Fluorouracil--pharmacology--PD; *Interferon Type II--pharmacology--PD; *Thymidylate Synthase--drug effects--DE; %Drug% Synergism; Enzyme Induction--%drug% effects--DE; Enzyme Stability--%drug% effects--DE; Gene %Expression% Regulation, Neoplastic--%drug% effects--DE; RNA, Messenger--%drug% effects--DE; RNA, Neoplasm--%drug% effects--DE; %Thymidylate% Synthase--biosynthesis--BI; %Thymidylate% Synthase--genetics--GE; Translation, Genetic--%drug% effects--DE; %Tumor% Cells, Cultured

CAS Registry No.: 0 (RNA, Messenger); 0 (RNA, Neoplasm); 51-21-8 (Fluorouracil); 82115-62-6 (Interferon Type II)

Enzyme No.: EC 2.1.1.45 (Thymidylate Synthase)

Record Date Created: 19930518

11/5/15 (Item 7 from file: 155)
DIALOG(R)File 155: MEDLINE(R)
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06911534 93090888 PMID: 1457523

Antimetabolites.

Chen AP; Grem JL

National Cancer Institute, Bethesda, Maryland.

Current opinion in oncology (UNITED STATES) Dec 1992, 4 (6) p1089-98

, ISSN 1040-8746 Journal Code: A1V

Languages: ENGLISH

Document type: Journal Article; Review; Review Literature

Record type: Completed

Subfile: INDEX MEDICUS

Research efforts over the past year further elucidate the determinants of sensitivity and mechanisms of resistance to the antimetabolites fluorouracil, methotrexate, and cytarabine. Progress has been made in clarifying the complex regulation of target enzyme %expression% for these antimetabolites. Advances in analytical methodology should facilitate quantitation of %thymidylate% synthase content in %tumor% tissue prior to and following fluorouracil-based %therapy%. Information concerning the basis for certain %drug% interactions may guide rational dose rates and schedules for clinical trials. A better understanding of the clinical pharmacology of these agents has suggested strategies to minimize their toxicity while maintaining therapeutic activity. (77 Refs.)

Tags: Animal; Human

Descriptors: *Cytarabine--therapeutic use--TU; *Fluorouracil--therapeutic use--TU; *Methotrexate--therapeutic use--TU; Drug Interactions; Drug Resistance; Fluorouracil--pharmacokinetics--PK; Fluorouracil--pharmacology--PD; Methotrexate--pharmacology--PD; Neoplasms--drug therapy--DT

CAS Registry No.: 147-94-4 (Cytarabine); 51-21-8 (Fluorouracil); 59-05-2 (Methotrexate)

Record Date Created: 19930111

11/5/16 (Item 1 from file: 399)
DIALOG(R)File 399: CA SEARCH(R)
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126246475 CA: 126(19)246475u JOURNAL

Thymidylate synthase expression and response to neoadjuvant chemotherapy in patients with advanced head and neck cancer

AUTHOR(S): Johnston, Patrick G.; Mick, Rosemarie; Recant, Wendy; Behan, Katherine A.; Dolan, M. Eileen; Ratain, Mark J.; Beckmann, Enrique; Weichselbaum, Ralph R.; Allegra, Carmen J.; Vokes, Everett E.

LOCATION: NCI-Navy Medical Oncology Branch, Division of Clinical Sciences, National Cancer Institute, Bethesda, MD, USA

JOURNAL: J. Natl. Cancer Inst. DATE: 1997 VOLUME: 89 NUMBER: 4

PAGES: 308-313 CODEN: JNCIEQ ISSN: 0027-8874 LANGUAGE: English

PUBLISHER: Oxford University Press

SECTION:

CA201006 Pharmacology

IDENTIFIERS: thymidylate synthase fluorouracil head neck cancer, chemotherapy thymidylate synthase fluororacil neck cancer

DESCRIPTORS:

Antitumor agents...

head; thymidylate synthase expression and response to neoadjuvant chemotherapy in patients with advanced head and neck cancer

Head...

neoplasm, inhibitors; thymidylate synthase expression and response to neoadjuvant chemotherapy in patients with advanced head and neck cancer

Drug resistance... Interferon .alpha.2b...

thymidylate synthase expression and response to neoadjuvant

chemotherapy in patients with advanced head and neck cancer

CAS REGISTRY NUMBERS:

51-21-8 58-05-9 59-05-2 9031-61-2 15663-27-1 72732-56-0 thymidylate synthase expression and response to neoadjuvant chemotherapy in patients with advanced head and neck cancer

11/5/17 (Item 2 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

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121292162 CA: 121(25)292162j JOURNAL

The role of P-glycoprotein, glutathione S-transferase-.pi., thymidylate synthase, and metallothionein in the expression of differential sensitivities to antitumor agents in human tumor xenografts

AUTHOR(S): Mattern, Juergen; Volm, Manfred

LOCATION: Deutsches Krebsforschungszentrum, Heidelberg, Germany, D-69120

JOURNAL: Oncol. Rep. DATE: 1994 VOLUME: 1 NUMBER: 5 PAGES: 927-32

CODEN: OCRPEW LANGUAGE: English

SECTION:

CA201006 Pharmacology

IDENTIFIERS: P-glycoprotein neoplasm inhibitor sensitivity, glutathione transferase pi antitumor agent sensitivity, thymidylate synthase neoplasm inhibitor sensitivity, metallothionein neoplasm inhibitor sensitivity

DESCRIPTORS:

Drug resistance... Glycophosphoproteins, P-... Metallothioneins... Neoplasm inhibitors...

P-glycoprotein, glutathione S-transferase-.pi., thymidylate synthase, and metallothionein role in expression of differential sensitivities to antitumor agents in human tumor xenografts

CAS REGISTRY NUMBERS:

50-18-0 50-76-0 51-21-8 57-22-7 148-82-3 9031-61-2 15663-27-1

23214-92-8 P-glycoprotein, glutathione S-transferase-.pi., thymidylate synthase, and metallothionein role in expression of differential sensitivities to antitumor agents in human tumor xenografts

50812-37-8 .pi.; P-glycoprotein, glutathione S-transferase-.pi., thymidylate synthase, and metallothionein role in expression of differential sensitivities to antitumor agents in human tumor xenografts

11/5/18 (Item 1 from file: 76)

DIALOG(R)File 76:Life Sciences Collection

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01556212 2675725

Quantitation of thymidylate synthase, dihydrofolate reductase, and DT-diaphorase gene expression in human tumors using the polymerase chain reaction.

Horikoshi, T.; Danenberg, K.D.; Stadlbauer, T.H.W.; Volkenandt, M.; Shea, L.C.C.; Aigner, K.; Gustavsson, B.; Leichman, L.; Danenberg, P.V.; et al. 1303 N. Mission Rd., Los Angeles, CA 90033, USA

CANCER RES. vol. 52, no. 1, pp. 108-116 (1992.)

DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH

SUBFILE: Biochemistry Abstracts Part 2: Nucleic Acids

A polymerase chain reaction (PCR)-based method was used to quantitate the expression levels of low abundance genes relevant to cancer %drug% activity. RNA from %tumor% samples as small as 20 mg was isolated and converted to cDNA using random hexamers. We measured the relative %expressions% of %thymidylate% synthase, dihydrofolate reductase, and DT-diaphorase in a number of clinical %tumor% samples. Those tumors with the lowest %thymidylate% synthase %expression% had the best response to both the 5-fluorouracil-leucovorin and 5-fluorouracil-cisplatin combinations.

DESCRIPTORS: thymidylate synthase; dihydrofolate reductase; DT-diaphorase
IDENTIFIERS: genes; gene expression; levels; determination; polymerase
chain reaction; tumours; man
SECTION HEADING: 14550 --General

11/5/19 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal
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13859025 PASCAL No.: 99-0036609
High basal level gene expression of thymidine phosphorylase
(platelet-derived endothelial cell growth factor) in colorectal tumors is
associated with nonresponse to 5-fluorouracil
METZGER R; DANENBERG K; LEICHMAN C G; SALONGA D; SCHWARTZ E L; WADLER S;
LENZ H J; GROSSEN S; LEICHMAN L; DANENBERG P V
USC/Norris Cancer Center, University of Southern California School of
Medicine, Los Angeles. California 90033, United States; Albert Einstein
Cancer Center, Bronx, New York 10467, United States
Journal: Clinical cancer research, 1998, 4 (10) 2371-2376
ISSN: 1078-0432 Availability: INIST-26073; 354000071337060110
No. of Refs.: 46 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: United States
Language: English

English Descriptors: Fluorouracil; Calcium folinate; %Drug% combination;
Gene %expression%; Thymidine phosphorylase; Malignant %tumor%; Colon;
Rectum; Human; %Thymidylate% synthase; Chemotherapy; Treatment efficiency
; Fluoropyrimidine derivatives; Pyrimidine derivatives; Antineoplastic
agent
Broad Descriptors: Pentosyltransferases; Glycosyltransferases; Transferases
; Enzyme; Methyltransferases; Digestive diseases; Intestinal disease;
Colonic disease; Rectal disease; Pentosyltransferases;
Glycosyltransferases; Transferases; Enzyme; Methyltransferases; Appareil
digestif pathologie; Intestin pathologie; Colon pathologie; Rectum
pathologie; Pentosyltransferases; Glycosyltransferases; Transferases;
Enzima; Methyltransferases; Aparato digestivo patologia; Intestino
patologia; Colon patologia; Recto patologia

French Descriptors: Fluorouracil; Folinate de calcium; Association
medicamenteuse; Expression genique; Thymidine phosphorylase; Tumeur
maligne; Colon; Rectum; Homme; Thymidylate synthase; Chimiotherapie;
Efficacite traitement; Fluoropyrimidine derive; Pyrimidine derive;
Anticancereux; Leucovorine

Classification Codes: 002B02R02

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11/5/20 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal
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13787522 PASCAL No.: 98-0501522
Mechanism and pharmacological specificity of dUTPase-mediated protection
from DNA damage and cytotoxicity in human tumor cells
PARSELS L A; PARSELS J D; WAGNER L M; LONEY T L; RADANY E H; MAYBAUM J
Department of Pharmacology, University of Michigan Medical School, Ann
Arbor, MI 48109-0504, United States; Department of Radiation Oncology,
University of Michigan Medical School, Ann Arbor, MI 48109-0504, United
States
Journal: Cancer chemotherapy and pharmacology, 1998, 42 (5) 357-362

ISSN: 0344-5704 CODEN: CCPHDZ Availability: INIST-16820;

354000070976530020

No. of Refs.: 22 ref.

Document Type: P (Serial) ; A (Analytic)

Country of Publication: Germany

Language: English

Purpose: We have reported previously that the expression of *E. coli* dUTPase (dutE) can protect HT29 cells from 5-fluorodeoxyuridine (FdUrd)-induced DNA fragmentation and cytotoxicity. In the study reported here, we further characterized the ability of dutE expression in one HT29 clone, dutE7, to alter the effects of treatment with FdUrd and other thymidylate synthase (TS) inhibitors. In addition, we developed two HuTu80 dutE-expressing clones using a pLN CX-dutE retroviral construct and tested their sensitivity to FdUrd-induced DNA fragmentation and cytotoxicity. **Methods:** Both a dutE retroviral expression system and a dutE antibody were developed to facilitate the generation and screening of dutE-expressing clones. HT29 and HuTu80 clones expressing dutE were tested for drug-induced DNA damage with either alkaline elution or pulsed field gel electrophoresis and drug-induced loss of clonogenicity. **Results:** Following a 24-h treatment with 100 μ M CB3717 or 500 nM methotrexate (MTX), dutE7 cells were significantly less sensitive to drug-induced loss of clonogenicity than con3 cells. DutE7 cells were also resistant to CB3717-induced DNA fragmentation at 24 h. However, following a 48-h treatment with CB3717 or MTX there was no difference in survival between con3 and dutE7 cells, even though DNA damage was still greatly attenuated in the dutE7 cell line. In addition, expression of dutE in two HuTu80 clones, 80 C and 80 K, did not protect these cells from FdUrd-induced DNA damage or cytotoxicity. **Conclusions:** We conclude that the role of uracil misincorporation and subsequent DNA damage in cytotoxicity induced by TS inhibitors, in HT29 cells, is time dependent, and that cytotoxicity caused by long-term exposure to these drugs is largely independent of resultant DNA damage, in this cell line. The inability of dutE to protect HuTu80 cells from FdUrd further suggests that the significance of uracil misincorporation resulting from TS inhibition varies among cell lines.

English Descriptors: Mechanism of action; Biological activity; Fluorouracil; Cytotoxicity; Human; Malignant %tumor%; Colon; Established cell line; %Tumor% cell; In vitro; Antineoplastic agent; Chemotherapy; Uracil; Negative %therapeutic% reaction; Gene product; Fluoropyrimidine derivatives; Gene %expression%; dUTP pyrophosphatase; %Thymidylate% synthase

Broad Descriptors: Digestive diseases; Intestinal disease; Colonic disease; Hydrolases; Enzyme; Methyltransferases; Transferases; Appareil digestif pathologie; Intestin pathologie; Colon pathologie; Hydrolases; Enzyme; Methyltransferases; Transferases; Aparato digestivo patologia; Intestino patologia; Colon patologia; Hydrolases; Enzima; Methyltransferases; Transferases

French Descriptors: Mecanisme action; Activite biologique; Fluorouracil; Cytotoxicite; Homme; Tumeur maligne; Colon; Ligne cellulaire etablie; Cellule tumorale; In vitro; Anticancereux; Chimiotherapie; Uracile; Resistance traitement; Produit gene; Fluoropyrimidine derive; Expression genique; dUTP pyrophosphatase; Thymidylate synthase; Ligne HT29

Classification Codes: 002B04H03

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11/5/21 (Item 3 from file: 144)
DIALOG(R)File 144:Pascal
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13668018 PASCAL No.: 98-0376021
Thymidine phosphorylase moderates thymidine-dependent rescue after exposure to the thymidylate synthase inhibitor ZD1694 (Tomudex) in vitro

PATTERSON A V; TALBOT D C; STRATFORD I J; HARRIS A L
Experimental Oncology Group, Department of Pharmacy, University of
Manchester, Manchester M13 9PL, United Kingdom; Imperial Cancer Research
Fund, Clinical Oncology Unit, Institute of Molecular Medicine, University
of Oxford, John Radcliffe Hospital, Oxford OX3 9DU, United Kingdom

Journal: *Cancer research* : (Baltimore), 1998, 58 (13) 2737-2740

ISSN: 0008-5472 CODEN: CNREA8 Availability: INIST-5088;

354000077102220110

No. of Refs.: 18 ref.

Document Type: P (Serial) ; A (Analytic)

Country of Publication: United States

Language: English

The inhibition of de novo thymidine (dThd) synthesis by the novel folate-based thymidylate synthase (TS) inhibitor ZD1694 (Tomudex) can achieve tumor cell-specific cytotoxicity *in vivo*. However, nucleosides in the surrounding microenvironment of tumors may be used by the salvage pathway to regenerate any depleted pools, thus providing an efficient mechanism through which to circumvent the ZD1694-dependent toxicity. Anabolism of dThd to dTMP by dThd kinase (TK) is the first committed step in the dThd salvage pathway. However, dThd phosphorylase (dThdPase) can compete with TK by catalyzing the reversible phosphorolytic cleavage of dThd to thymine and deoxyribose 1-phosphate and rendering the salvaged dThd metabolically unavailable. Both TK and dThdPase are up-regulated in some tumors, and their relative importance is not fully defined. We have studied the influence of dThdPase expression on the capacity of exogenous dThd to reverse ZD1694-dependent growth inhibition and have shown that both intra- and extracellular dThdPase activity can effectively moderate dThd-rescue. This suggests that tumor levels of dThdPase may be an important factor in the outcome of ZD1694 therapy.

English Descriptors: Enzyme inhibitor; Enzymatic activity; Cytotoxicity; Cytostase; Gene %expression%; Adenocarcinoma; Mammary gland; Gene product ; In vitro; Established cell line; %Tumor% cell; Negative %therapeutic% reaction; Human; Female; %Thymidylate% synthase; Thymidine kinase; Thymidine phosphorylase

Broad Descriptors: Methyltransferases; Transferases; Enzyme; Malignant tumor; Mammary gland diseases; Pentosyltransferases; Glycosyltransferases ; Methyltransferases; Transferases; Enzyme; Tumeur maligne; Glande mammaire pathologie; Pentosyltransferases; Glycosyltransferases; Methyltransferases; Transferases; Enzima; Tumor maligno; Glandula mamaria patologia; Pentosyltransferases; Glycosyltransferases

French Descriptors: Inhibiteur enzyme; Activite enzymatique; Cytotoxicite; Cytostase; Expression genique; Adenocarcinome; Glande mammaire; Produit gene; In vitro; Ligne cellulaire etablie; Cellule tumorale; Resistance traitement; Homme; Femelle; Thymidylate synthase; Thymidine kinase; Thymidine phosphorylase; Tomudex; ZD 1694; Ligne MCF7

Classification Codes: 002B02R02

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11/5/22 (Item 4 from file: 144)
DIALOG(R)File 144:Pascal
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13667477 PASCAL No.: 98-0375454
Variable expression of RFC1 in human leukemia cell lines resistant to
antifolates
KOBAYASHI H; TAKEMURA Y; OHNUMA T
Department of Laboratory Medicine, National Defense Medical College, 3-2,
Namiki, Tokorozawa, Saitama 359, Japan; Division of Neoplastic Diseases,
Samuel Bronfman Department of Medicine, Mount Sinai School of Medicine, One

Gustave L. Levy Place, New York, NY 10029, United States
Journal: Cancer letters, 1998, 124 (2) 135-142
ISSN: 0304-3835 CODEN: CALEDO Availability: INIST-17217;
354000076858530030

No. of Refs.: 33 ref.

Document Type: P (Serial) ; A (Analytic)

Country of Publication: Ireland

Language: English

The resistance to folate-based antifolates is associated with impaired function of the reduced folate carrier (RFC), one of the major routes of folate transport into cancer cells. To clarify the importance of RFC functions in the antifolate resistance, we have examined the expression of RFC1 and its phenotype as a folate transporter in human leukemia cell lines resistant to various antifolates. MOLT-3 cells resistant to ZD9331 (a thymidylate synthase (TS) inhibitor that utilizes the RFC for cell entry) (MOLT-3/ZD9331) showed decreased expression of RFC1 concomitant with diminished cellular uptake of (SUP 3 H)methotrexate (MTX). K562 cells resistant to raltitrexed (ZD1694, another TS inhibitor that utilizes the RFC for cell entry) (K562/ ZD1694.C) scarcely expressed RFC1, which is in accordance with the impaired uptake of folate analogs and the high degree of resistance to ZD1694 and MTX. On the other hand, no apparent decrease of RFC1 expression was found in transport-deficient MTX-resistant MOLT-3 cells (MOLT-3/MTX SUB 1 SUB 0 SUB 0 SUB 0 SUB 0) though its phenotype showed defective transport of MTX or ZD1694. In these cell lines with impaired RFC function, (SUP 3 H)leucovorin (LV) uptake was only moderately decreased as compared to (SUP 3 H)MTX or (SUP 3 H)ZD1694 uptake. These cells grew with a minimal retardation in folate-free medium supplemented with 10 nM LV, suggesting that these cell lines with impaired RFC function had enough folate transporters to transport LV. In contrast to downregulation of RFC, the much greater uptake of (SUP 3 H)MTX was observed in the MOLT-3/ trimetrexate (TMQ) SUB 8 SUB 0 SUB 0 -MTX SUB 1 SUB 0 SUB 0 SUB 0 SUB 0 in parallel with increased RFC1 expression. These cell lines with the altered expression of RFC1 may serve as models useful for investigating the regulation of RFC1 expression and for understanding the molecular mechanism(s) behind the transport-mediated antifolate resistance.

English Descriptors: Calcium folinate; Trimetrexate; Methotrexate; Leukemia ; Human; Established cell line; %Tumor% cell; In vitro; Negative %therapeutic% reaction; Intracellular transport; Gene product; Antifolate ; Gene %expression%; Antineoplastic agent; Chemotherapy; %Thymidylate% synthase

Broad Descriptors: Malignant hemopathy; Methyltransferases; Transferases; Enzyme; Hemopathie maligne; Methyltransferases; Transferases; Enzyme; Hemopatia maligna; Methyltransferases; Transferases; Enzima

French Descriptors: Folinate de calcium; Trimetrexate; Methotrexate; Leucemie; Homme; Ligne cellulaire etablie; Cellule tumorale; In vitro; Resistance traitement; Transport intracellulaire; Produit gene; Antifolate; Expression genique; Anticancereux; Chimiotherapie; Thymidylate synthase; Gene RFC1

Classification Codes: 002B19B

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11/5/23 (Item 5 from file: 144)
DIALOG(R) File 144:Pascal
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13610261 PASCAL No.: 98-0315637

Molecular characterization of human acute leukemia cell line resistant to ZD9331, a non-polyglutamatable thymidylate synthase inhibitor
KOBAYASHI H; TAKEMURA Y; MIYACHI H
Department of Laboratory Medicine, National Defense Medical College, 3-2,

Namiki, Tokorozawa, Saitama 359-0042, Japan; Department of Clinical Pathology, Tokai University School of Medicine, Bohseidai, Isehara, Kanagawa 259-1193, Japan

Journal: Cancer chemotherapy and pharmacology, 1998, 42 (2) 105-110

ISSN: 0344-5704 CODEN: CCPHDZ Availability: INIST-16820;

354000076427060030

No. of Refs.: 24 ref.

Document Type: P (Serial) ; A (Analytic)

Country of Publication: Germany

Language: English

ZD9331 is a non-polyglutamatable, potent quinazoline antifolate inhibitor of thymidylate synthase (TS). In an effort to clarify the exact mechanism of resistance to this novel TS inhibitor, we examined the molecular alterations in its target enzyme TS, the transport protein (reduced folate carrier, RFC), and folylpolyglutamate synthetase (FPGS) in a human acute lymphoblastic leukemia cell line, MOLT-3, made resistant to ZD9331. A 310-fold resistant subline was established after 6 months exposure to the drug at concentrations up to 7 μ M, and was designated MOLT-3/ZD9331. MOLT-3/ZD9331 showed crossresistance to CB3717 (4.8-fold), raltitrexed (63-fold) and methotrexate (MTX) (120-fold), but retained sensitivity to trimetrexate (0.88-fold). The resistant cells demonstrated impaired initial cellular uptake and low accumulation of (³H)MTX in accordance with a decreased expression of RFC1, suggesting the downregulation of RFC. However, Southern blot analysis demonstrated no change in gene copy number nor gross rearrangement of RFC1 in the resistant cells. In addition, MOLT-3/ZD9331 showed amplification of the TS gene with a concomitantly increased level in the gene expression. In contrast, the expression of FPGS did not alter. These results

English Descriptors: Enzyme inhibitor; Methotrexate; Cross resistance; Chemotherapy; Human; Acute lymphocytic leukemia; Established cell line; %Tumor% cell; In vitro; Negative %therapeutic% reaction; Antineoplastic agent; Treatment; Gene %expression%; Gene product; Acute; %Thymidylate% synthase

Broad Descriptors: Malignant hemopathy; Lymphoproliferative syndrome; Methyltransferases; Transferases; Enzyme; Hemopathie maligne; Lymphoproliferatif syndrome; Methyltransferases; Transferases; Enzyme; Hemopatia maligna; Linfoproliferativo sindrome; Methyltransferases; Transferases; Enzima

French Descriptors: Inhibiteur enzyme; Methotrexate; Resistance croisée; Chimiotherapie; Homme; Leucemie lymphoblastique; Ligne cellulaire établie; Cellule tumorale; In vitro; Resistance traitement; Anticancereux ; Traitement; Expression génique; Produit gene; Aigu; Thymidylate synthase; ZD 9331; Raltixered; Ligne MOLT3; CB 3717

Classification Codes: 002B02R02

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11/5/24 (Item 6 from file: 144)

DIALOG(R)File 144:Pascal

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13576213 PASCAL No.: 98-0278803

p53 point mutations and thymidylate synthase messenger RNA levels in disseminated colorectal cancer : An analysis of response and survival
LENZ H J; HAYASHI K; SALONGA D; DANENBERG K D; DANENBERG P V; METZGER R;
BANERJEE D; BERTINO J R; GROSHER S; LEICHMAN L P; LEICHMAN C G
University of Southern California/Norris Comprehensive Cancer Center,
University of Southern California School of Medicine, Los Angeles,
California 90033, United States; Memorial Sloan-Kettering Cancer Center,
New York, New York 10021, United States

Journal: Clinical cancer research, 1998, 4 (5) 1243-1250
ISSN: 1078-0432 Availability: INIST-26073; 354000075848580200
No. of Refs.: 41 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: United States
Language: English

English Descriptors: Malignant %tumor%; Colon; Rectum; Disseminated; Point mutation; TP53 Gene; %Thymidylate% synthase; Messenger RNA; Gene %expression%; Fluorouracil; Antineoplastic agent; Negative %therapeutic% reaction; Treatment; Chemotherapy; Treatment efficiency; Survival; Human; Fluoropyrimidine derivatives

Broad Descriptors: Methyltransferases; Transferases; Enzyme; Digestive diseases; Intestinal disease; Colonic disease; Rectal disease; Genetics; Methyltransferases; Transferases; Enzyme; Appareil digestif pathologie; Intestin pathologie; Colon pathologie; Rectum pathologie; Genetique; Methyltransferases; Transferases; Enzima; Aparato digestivo patologia; Intestino patologia; Colon patologia; Recto patologia; Genetica

French Descriptors: Tumeur maligne; Colon; Rectum; Dissemine; Mutation ponctuelle; Gene TP53; Thymidylate synthase; RNA messager; Expression genique; Fluorouracil; Anticancereux; Resistance traitement; Traitement; Chimiotherapie; Efficacite traitement; Survie; Homme; Fluoropyrimidine derivee

Classification Codes: 002B13B01

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11/5/25 (Item 7 from file: 144)
DIALOG(R)File 144:Pascal
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10001530 PASCAL No.: 92-0223816
Quantitation of thymidylate synthase, dihydrofolate reductase, ant DT-diaphorase gene expression in human tumors using the polymerase chain reaction

HORIKOSHI T; DANENBERG K D; STADBAUER T H W; VOLKENANDT M; SHEA L C C; AIGNER K; GUSTAVSSON B; LEICHMAN L; FROSING R; RAY M; GIBSON N W; SPEARS C P; DANENBERG P V

Univ. southern California school medicine, Kenneth Norris Jr cancer hosp., res. inst., Los Angeles CA 90033, USA

Journal: Cancer research : (Baltimore), 1992, 52 (1) 108-116

ISSN: 0008-5472 CODEN: CNREA8 Availability: INIST-5088;

354000023207790180

No. of Refs.: 24 ref.

Document Type: P (Serial) ; A (Analytic)

Country of Publication: USA

Language: English Summary Language: English

A polymerase chain reaction (PCR)-based method was used to quantitate the expression levels of low abundance genes relevant to cancer drug activity. RNA from tumor samples as small as 20 mg was isolated and converted to cDNA using random hexamers. The 5' primers for the PCR contained a T7 polymerase promoter sequence, allowing the PCR-amplified DNA to be transcribed to RNA fragments. In each sample, the linear ranges of amplification of each cDNA of interest were established

English Descriptors: Malignant %tumor%; Human; Exploration; %Thymidylate% synthase; Tetrahydrofolate dehydrogenase; NADPH dehydrogenase (quinone); Gene %expression%; Quantitative analysis; Polymerase chain reaction; Complementary DNA; Chemotherapy; %Drug% combination; Treatment; Antineoplastic agent

Broad Descriptors: Enzyme; Enzyme; Enzima

French Descriptors: Tumeur maligne; Homme; Exploration; Thymidylate synthase; Tetrahydrofolate dehydrogenase; NADPH dehydrogenase (quinone); Expression genique; Analyse quantitative; Reaction chaine polymerase; DNA complementaire; Chimiotherapie; Fluorouracil; Association medicamenteuse; Leucovorine; Traitement; Anticancereux

Classification Codes: 002B04C

11/5/26 (Item 8 from file: 144)
DIALOG(R)File 144:Pascal
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08434825 PASCAL No.: 88-0435713
Biochemical and molecular properties of cisplatin-resistant A2780 cells grown in folinic acid
YING LU; JUI HAN; SCANLON K J
City of Hope national medical cent., dep. medical oncology, Duarte CA 91010, USA
Journal: Journal of biological Chemistry, 1988, 263 (10) 4891-4894
ISSN: 0021-9258 CODEN: JBCHA3 Availability: CNRS-3082
No. of Refs.: 29 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: USA
Language: ENGLISH

English Descriptors: Folic acid; Cell culture; %Tumor%; Ovary; Human; Folic acid; Resistance; %Drug%; Transportation system; Aminoacid; Enzyme; Tetrahydrofolate dehydrogenase; Messenger RNA; Northern blotting; %Thymidylate% synthase; Gene %expression%; Metabolism

French Descriptors: Folique acide; Culture cellulaire; Tumeur; Ovaire; Homme; Folique acide; Resistance; Medicament; Systeme transport; Aminoacide; Enzyme; Tetrahydrofolate dehydrogenase; RNA messager; Methode Northern; Thymidylate synthase; Expression genique; Metabolisme; Ligne A2780; Cisplatine; DTMP synthase

Classification Codes: 002A04H01

11/5/27 (Item 1 from file: 94)
DIALOG(R)File 94:JICST-EPlus
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02538453 JICST ACCESSION NUMBER: 95A0629430 FILE SEGMENT: JICST-E
Applications of the Most Updated Biomedical Technology to Pathophysiology and Laboratory Medicine. Rapid Diagnosis of Drug-Resistant Genes by PCR Assay.
FUNATO TADAO (1)
(1) Tohoku Univ., Sch. of Med.
Rinsho Byori (Japanese Journal of Clinical Pathology), 1995, VOL.43, NO.6, PAGE.535-539, FIG.2, TBL.3, REF.10
JOURNAL NUMBER: Z0687AAS ISSN NO: 0047-1860 CODEN: RBYOA
UNIVERSAL DECIMAL CLASSIFICATION: 616-006-09 616-09
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Review article
MEDIA TYPE: Printed Publication
ABSTRACT: This report concerns the utility of the reverse transcription-polymerase chain reaction (RT-PCR) and quantitative PCR (QPCR) assay to detect the %drug%-resistance of related genes. The expression of some %drug%-resistance genes was compared with the

sensitivity and resistance-acquired %cancer% cell lines to anti-%cancer% drugs by Northern blot analysis and PCR assay. The resistance cell lines exhibited an enhanced %expression% of multi-%drug% resistance(MDR-1), %thymidylate% synthase(TS), c-fos and DNA polymerase .BETA. genes. Then these genes that %expressed% mRNA were quantitated using RT-PCR. The expression of the genes was dependent on their sensitivity (IC50) to anti-%cancer% drugs. Additionally, the QPCR assay has been developed as a rapid method for the expression of %drug%-resistance genes and applied to the PCR products amplified by the RT-PCR. Thus the QPCR assay for the expression of genes will allow rapid detection of the drug-resistance to chemotherapy in human cancers. (author abst.)

DESCRIPTORS: drug resistance; polymerase chain reaction; gene diagnosis; gene expression; early diagnosis; multiple drug resistance; drug resistance factor; dichlorodiammine platinum; quantitative analysis; tumor cell; human(primates)

BROADER DESCRIPTORS: resistance(endure); genetic technique; technology; DNA diagnosis; diagnosis; molecular genetic phenomenon; genetic phenomenon; phenomenon; factor; plasmid; ammine complex; complex(compound); coordination compound; compound(chemical); nitrogen compound; nitrogen group element compound; chloro complex; chloride; chlorine compound; halogen compound; halide; halogeno complex; antitumor drug; drug; platinum complex; platinum compound; platinum group element compound; transition metal compound; platinum group element complex; transition metal complex; metal complex; analysis(separation); analysis; idioblast ; cell(cytology)

CLASSIFICATION CODE(S): GE02030N; GC02040S

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